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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,066	12/07/2001	John J. L. Simard	0088480-021US1	8425

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,066	SIMARD ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,29-36,40-52 and 54-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,29-36,40-52 and 54-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 10/005,905 (ABN); which is a continuation-in-part of U.S. Application Serial Numbers 09/561,074 (now U.S. Patent No. 6,861,234), 09/560,465 (ABN) and 09/561,572 (ABN); and is a continuation-in-part of PCT Serial Number PCT/US01/13806. The priority date of this application is April 27, 2000.

Claims 6-28, 37-39 and 53 have been canceled.

Claims 1-5, 29-36, 40-52 and 54-59 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment and remarks filed December 31, 2008, no outstanding grounds of rejection are maintained. The following represent NEW GROUNDS of rejection that were not necessitated by the amendment. Accordingly, this Office Action is made NON-FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-5, 29, 30, 33-35 and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zajac et al (145 on form PTO-1449; Int. J. Cancer [1997] 71:491-496, of record) in view of Kawakami et al (J. Immunother. [1998] 21(4):237-246; 77 on form PTO-1449 filed 12/9/2002, newly cited).

Zajac teaches isolated T cells that recognize the HLA-A2.1-restricted housekeeping epitope consisting of amino acid residues 27-35 of the MelanA tumor-associated antigen from melanoma target

cells (Abstract and page 491, first column in particular)[claims 1, 3, 29, 30, 33-35]. Zajac teaches that tumor-infiltrating-lymphocytes (TILs) were isolated from melanoma patients were able to specifically lyse target cells (pages 492-493 and Figure 2 in particular). The TILs qualify as being "isolated from an immunized animal" because they were obtained from melanoma patients and were therefore "immunized" to the antigen by the presence of the tumor in their body [claim 5]. Accordingly, prior to transformation of the cell line the reactive T cells were present in human serum, a carrier suitable for administration to a human. The composition satisfies the metes and bounds of the claimed composition. Zajac discusses the use of the MART-1/MelanA_{27-35} peptide as an active immunogen in cancer patients (Abstract and page 495, column 2 in particular)

Claims 40 and 41 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Kawakami teaches that "[t]umor-reactive T cells that have been activated in vivo can then be further expanded by *in vitro* culture with IL-2 and used for adoptive immunotherapy" (page 239, second column in particular). Accordingly, it would have been well within the purview of the artisan at the time the invention was made to expand tumor-reactive T cells in in vitro culture and make the cells suitable for administration as an adoptive immunotherapeutic reagent. Like Zajac, Kawakami also discusses the use of the MART-1/MelanA_{27-35} peptide as an active immunogen, referring to clinical protocols (Table 4 in particular). However, Kawakami also teaches that potent melanoma-reactive T cells can be induced from the peripheral lymphocytes of cancer patients or from subjects immunized with the peptides [claim 5] and useful for adoptive transfer protocols (page 242, column 2 to page 243, column 1 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use expanded T cells from the cells isolated T cells of Zajac as an adoptive immunotherapeutic. One would have been motivated to formulate a therapeutic preparation suitable for use in humans comprising these cells with a reasonable expectation of success by the teachings of Kawakami that cells expanded in vitro with substances such as IL-2 can still be used for adoptive transfer to human subjects.

2. Claims 1-5, 29, 30, 33, 34, 36 and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kittlesen et al (79 on form PTO-1449; J. Immunol. [1998] 160:2099-2106, of record) in view of Kawakami et al (J. Immunother. [1998] 21(4):237-246; 77 on form PTO-1449 filed 12/9/2002, newly cited).

Kittlesen teaches isolated T cell lines that recognize the HLA-A1-restricted housekeeping epitope consisting of the amino acid sequence KCDICTDEY of the tyrosinase tumor-associated antigen from melanoma target cells (Abstract, page 2100, first column in particular, page 2101, second column in particular)[claims 1, 29, 30, 33, 34, 36]. Kittlesen teaches that the tyrosine reactive T cells are obtained from melanoma patients whose tumors express tyrosinase (paragraph bridging pages 2100-2101 in particular) and therefore qualify as being "isolated from an immunized animal" because they were obtained from melanoma patients and were therefore "immunized" to the antigen by the presence of the tumor in their body [claim 5]. Accordingly, prior to transformation of the cell line the reactive T cells were present in human serum, a carrier suitable for administration to a human. The composition satisfies the metes and bounds of the claimed composition. Kittlesen further teaches that the T cell lines were enriched in vitro from polyclonal populations [claim 3] obtained from melanoma patients by repeated rounds of stimulation with the peptide (page 2100, first column in particular) [claims 2, 4].

Claims 40 and 41 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Kawakami teaches that "[t]umor-reactive T cells that have been activated in vivo can then be further expanded by in vitro culture with IL-2 and used for adoptive immunotherapy" (page 239, second column in particular). Accordingly, it would have been well within the purview of the artisan at the time the invention was made to expand tumor-reactive T cells in in vitro culture and make the cells suitable for administration as an adoptive immunotherapeutic reagent. Like Kittlesen, Kawakami also discusses the use of the peptide epitopes as an active immunogen, referring to clinical protocols (Table 4 in particular). Furthermore, Kawakami also discloses the generation of T cells reactive with tyrosinase epitopes (table 3 in particular). Kawakami also teaches that potent tumor-reactive T cells can be induced from the peripheral lymphocytes of cancer patients or from subjects immunized with the peptides [claim 5] and useful for adoptive transfer protocols (page 242, column 2 to page 243, column 1 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use expanded T cells from the cells isolated T cells of Kittlesen as an adoptive immunotherapeutic. One would have been motivated to formulate a therapeutic preparation suitable for use in humans comprising these cells with a reasonable expectation of success by the teachings of Kawakami that cells expanded in vitro with substances such as IL-2 can still be used for adoptive transfer to human subjects.

3. Claims 1-5, 29-32, 35 and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jager et al (75 on form PTO-1449; J. Exp. Med. [1998] 187:265-270, of record) in view of Kawakami et al (J. Immunother. [1998] 21(4):237-246; 77 on form PTO-1449 filed 12/9/2002, newly cited).

Jager teaches isolated CD4+ T cell lines and an HLA-A2 restricted CTL clonal line that recognize housekeeping epitopes of the NY-ESO-1 cancer-testis tumor-associated antigen (Abstract and page 266, first column in particular)[claims 1-3, 29-32, 35]. Jager teaches that the NY-ESO-1 reactive T cells are obtained from PBL from a melanoma patient. Jager teaches that the T cells are obtained from a melanoma patient and therefore qualify as being "isolated from an immunized animal" because they were obtained from a melanoma patient that was therefore "immunized" to the antigen by the presence of the tumor in the body [claim 5].

Claims 40 and 41 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Kawakami teaches that "[t]umor-reactive T cells that have been activated in vivo can then be further expanded by in vitro culture with IL-2 and used for adoptive immunotherapy" (page 239, second column in particular). Accordingly, it would have been well within the purview of the artisan at the time the invention was made to expand tumor-reactive T cells in in vitro culture and make the cells suitable for administration as an adoptive immunotherapeutic reagent. Jager teaches that NY-ESO-1 peptide can be used as an active immunogen as a vaccine preparation (page269, column 2 in particular). Kawakami also discusses the use of peptide epitopes as an active immunogen, referring to clinical protocols (Table 4 in particular). Kawakami also teaches that potent tumor-reactive T cells can be induced from the peripheral lymphocytes of cancer patients or from subjects immunized with the peptides [claim 5] and useful for adoptive transfer protocols (page 242, column 2 to page 243, column 1 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use expanded T cells from the cells isolated T cells of Jager as an adoptive immunotherapeutic. One would have been motivated to formulate a therapeutic preparation suitable for use in humans comprising these cells with a reasonable expectation of success by the teachings of Kawakami that cells expanded in vitro with substances such as IL-2 can still be used for adoptive transfer to human subjects.

4. Claims 45-52 and 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zajac et al (145 on form PTO-1449; Int. J. Cancer [1997] 71:491-496, of record) in view of Kawakami et al (J. Immunother. [1998] 21(4):237-246; 77 on form PTO-1449 filed 12/9/2002, newly cited), Jager et al (75

on form PTO-1449; J. Exp. Med. [1998] 187:265-270, of record) and Tsuji et al (Int. J. Immunopharmacology [1998] 20(1-3):111—124 (newly cited; U on form PTO-892).

Zajac, Kawakami and Jager have been discussed supra.

The references each teach the generation of T cells specific for tumor associated antigens in melanoma patients [claims 42, 44-47]. Zajac specifically teaches the generation of A2-restricted T cells reactive with the melanoma differentiation antigen Melan-A [claims 50-52]. Jager specifically teaches the generation of T cells specific for the cancer-testis antigen NY-ESO [claims 48, 49]. Kawakami teaches the in vitro generation of T cell clones suitable for adoptive administration to a human [claim 43].

The combined references do not specifically teach immunizing a subject against more than one epitope.

Tsuji teaches immunizing a subject with multiple peptides derived from B16 melanoma cells (Abstract in particular). Tsuji teaches that the peptides were acid eluted from cultured tumor cells. acid elution removes peptides from MHC class I on the surface of the cells (page 112 in particular), meaning that these peptides from non-immune cells are the product of processing by standard proteasomes and therefore are housekeeping epitopes. As these peptides are derived from whole cell elutions, the preparations comprise housekeeping epitopes from both different antigens (claims 45-52) and from same antigens (claims 54-59) of the tumor cells.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to treat a subject with T cells specific for more than one housekeeping epitope at the same time when the housekeeping epitopes are derived from the same or different antigens of the tumor. one would have been motivated to combine the teachings for such a combination therapy with a reasonable expectation of success by the teachings of Tsuji showing that treating a subject with multiple peptides inhibited tumor growth and promoted survival of treated subjects and by the fact that not only do both Zajac and Jager teach the expansion of housekeeping epitope specific T cells in vitro, which Kawakami teaches can be expanded for adoptive immunotherapy, but they also teach the use of these peptides for active therapy in subjects, providing a nexus to the peptide therapy taught by Tsuji.

Conclusion

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is 571-272-0852. The examiner can normally be reached on Mon.-Fri. 7:30 am to 4:00 pm ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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July 15, 2009

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